Running Phthalates to Ground

Pinpointing Exposure Sources in a Virtual Home

Methods to measure concentrations of chemicals in adults and children, a science known as biomonitoring, can be costly and burdensome. And, although biomonitoring data provide useful aggregate information on exposure to all sources, it is almost impossible to tell how much comes from a specific source. A new mechanistic model may offer a way to identify the strongest sources of exposure to semivolatile organic compounds by showing how chemicals move from a single product through a home and which model parameters have the greatest influence on exposure [***EHP* 118:253–258; Xu et al.**].

Researchers created a model of a hypothetical three-room house equipped with adjustable airflow systems to illustrate how human exposure to phthalates released by a specific source—in this case, vinyl flooring—might be predicted. Phthalates are plasticizers that are used in products as diverse as nail polish, plastic wiring, and children's toys. Data from the Centers for Disease Control and Prevention suggest that more than three-quarters of the U.S. population may be exposed to these suspected endocrine disruptors.

The research team built on an earlier model that described how diethylhexyl phthalate (DEHP)—one of the most prevalent phthalates—is released from vinyl flooring into air and sorbs strongly to interior surfaces (walls, ceilings, floors, furniture, etc.) and suspended particles. Here the researchers used the model to explore the relative importance of inhalation of vapor, inhalation of particles, dermal sorption of DEHP, and oral ingestion of household dust on total exposure levels. To test which parameters might change the amount of total DEHP exposure through different routes, the researchers varied model parameters such as the amount of ventilation and velocity of air moving through their model house.

Exposure to gas-phase phthalates from vinyl flooring can occur through ingestion, inhalation, or dermal absorption.

For example, they calculated that a fan pushing air through the house would cause more skin contact with phthalates by increasing the release rate from the vinyl surfaces to the air. The fan also thinned the layer of air cushioning the skin, increasing the transfer of DEHP from air to skin. Stagnant air without the fan caused less transfer of DEHP from air to skin, thus protecting against dermal uptake of DEHP.

The new model suggests that levels of phthalates measured in adults and children may result in part from contact with surfaces that may absorb high concentrations of DEHP, such as clothing. Changing the variables in the model house—from airflow to the amount of DEHP in the vinyl flooring to square footage in a room—made a difference in estimated exposure levels. Varying the parameters in this simple model demonstrated the potential for DEHP exposures arising from a single product to differ by as much as 40 times from one situation to another. That variability underscores the wide range of possible exposures across the population—and the difficulty of relying on biomonitoring alone to identify the most harmful sources.

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Traffic Marker?

Early Exposure to Air Pollution Associated with Childhood Asthma

Asthma is now the most common chronic disease for children and a major cause of emergency room visits, hospitalizations, and school absences, according to the World Health Organization. Now a large population-based study has shown an association between elevated exposure to air pollution *in utero* and during the first year of life and a higher risk of asthma in preschool-aged children [***EHP* 118:284–290; Clark et al.**].

There are multiple known risk factors for developing asthma, including genetic factors, diet, and exposure to secondhand tobacco smoke and allergens. The speed with which the disease has risen in most developed and developing countries suggests environmental exposures probably play a prominent role. Although air pollution is known to worsen existing asthma, a succession of recent studies is building evidence for an additional association between exposure to traffic-related air pollution and initial onset of asthma in children.

Using a nested case–control study design, researchers looked at administrative and health care data for nearly 3,500 children born in southwest British Columbia, Canada, in 1999 and 2000 who were diagnosed with asthma by age 4 years. Each case was age- and sex-matched to 5 randomly chosen controls born in the same region and time period.

To estimate air pollutant exposures, the researchers mapped the residential history of each child against air pollution data obtained from regulatory monitoring, land use regression modeling, and proximity to stationary pollution sources and to roads. These metrics were used to calculate average exposures for the duration of the mother's pregnancy and the child's first year of life. Nine pollutant exposures were evaluated: carbon monoxide, nitric oxide, nitrogen dioxide, particulate matter (PM_{10} and $PM_{2.5}$), ozone, sulfur dioxide, black carbon, and wood smoke.

The highest risk of asthma was associated with exposure to the traffic-related pollutants carbon monoxide, nitric oxide, nitrogen dioxide, and black carbon; lesser associations were seen with exposure to PM_{10} and sulfur dioxide, as well as with proximity to industrial point sources. Proximity to roads was not associated with increased risk, but only a small number of children resided near major roads in the study population. Associations between air pollution and asthma were generally greater in girls than in boys, although asthma was significantly more common in boys, consistent with other populations. The authors observe that other researchers also have reported stronger associations in girls, although the finding is not entirely consistent.

This is one of the few studies to examine the effect of *in utero* exposure on pediatric asthma risk. However, because of relatively high correlation between *in utero* and first-year exposures, the relative importance of these periods could not be discerned.

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To Each His Own

DEHP Yields Species-Specific Metabolic Phenotypes

Endocrine disruptors have been shown to disturb the balance between energy expenditure and storage in cellular models, a balance that is critical for proper metabolic functioning. Peroxisome proliferator–activated receptors (PPARs), potential molecular targets of endocrine disruptors in several tissues and organs, hold a key position as lipid sensors that direct metabolic gene expression. A new mouse study illustrates activation of a specific PPAR isotype with exposure to the endocrine disruptor diethylhexyl phthalate (DEHP) and provides evidence that the potential influence of DEHP exposure on diet-induced obesity may vary between species [***EHP* 118:234–241; Feige et al.**].

DEHP is a widely used industrial plasticizer that can leach from diverse consumer products including food packaging and medical devices such as plastic tubing and bags. When ingested, DEHP is converted to monoethylhexyl phthalate (MEHP), which is readily absorbed. Previous *in vitro* research has demonstrated that MEHP can activate all three PPAR isotypes (PPARα, PPARβ, and PPARγ). The result *in vivo* can be opposing effects depending on which isotype is activated: induction of adipogenesis (PPARγ) or fatty acid oxidation (PPARα, PPARβ).

To determine the physical and biochemical effects of DEHP exposure, weanling mice were fed regular diets, with treatment groups receiving either 100 mg DEHP/kg/day (low dose) or 1,000 mg DEHP/kg/day (high dose) in the chow. Food intake and physical activity did not differ between groups, and lean body mass was not affected. However, in DEHP-treated mice fat reserves were reduced, and blood tests indicated increased hepatic fatty acid oxidation. As a result, mice in the high-dose group gained 15% less weight than low-dose and control mice over the 10-week treatment period.

In a separate experiment, adult mice were fed a high-fat diet for 13 weeks. Fat mass increased from a baseline 8–10% of body mass to 30% in untreated mice but remained unchanged in mice receiving 500 mg DEHP/kg/day. Further experiments investigating the pattern of PPAR target gene expression and using mice lacking either PPARα or PPARβ revealed that DEHP effects were mediated through PPARα in the liver.

Finally, to make the model more applicable to humans, mice genetically engineered to carry human PPARα were exposed to DEHP. Interestingly, MEHP did not protect these mice from diet-related obesity as it did in wild-type mice; in fact, MEHP led to these mice being even more obese than controls. If this relationship holds true in humans, exposure to certain endocrine disruptors could potentially contribute to obesity by promoting fat accumulation.

Conclusions drawn from this study include the identification of hepatic PPARα as a key site for DEHP-associated disruption. The doses applied in this study are 2–3 orders of magnitude higher than estimated typical human exposures when normalized to body mass. However, the observation of subtle, species-specific differences in metabolic response to DEHP point to an important factor that should be considered as the biological effects of DEHP on human health are further explored.

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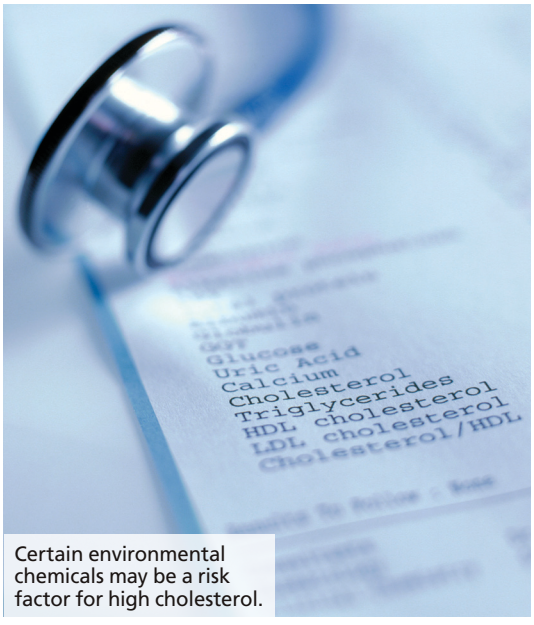
PFCs and Cholesterol

A Sticky Connection

Polyfluoroalkyl chemicals (PFCs), highly stable compounds used in consumer items such as food packaging, textiles, and paper products, are known to migrate throughout and persist in the environment. Animal studies have described the development of adverse health effects such as tumors and developmental delays with exposure to the PFCs perfluorooctanoic acid (PFOA) and perfluorooctane sulfonic acid (PFOS). A new study now suggests these and other PFCs may affect serum cholesterol levels in humans [***EHP* 118:197–202; Nelson et al.**].

Elevated cholesterol levels are associated with an increased risk of cardiovascular disease, and are one of the conditions that define metabolic syndrome. Risk factors for high cholesterol include diet, low physical activity, and a family history of the condition, but increasing evidence indicates some environmental chemicals also may contribute. With estimated half-lives of up to 8.5 years, PFCs are classified as persistent organic pollutants (POPs). However, unlike most POPs, which are stored primarily in fat tissue, PFCs persist by forming chemical bonds to proteins in the liver and serum.

Previous studies in humans have reported positive associations between PFOS and PFOA exposures and higher cholesterol levels. The research team in the current study investigated the relationship between insulin resistance, cholesterol levels, body size, and exposure to two less studied PFCs, perfluorononanoic acid (PFNA), and perfluorohexane sulfonic acid (PFHxS) in addition to PFOS and PFOA. The study used data from the 2003–2004 National Health and Nutrition Examination Survey.



Certain environmental chemicals may be a risk factor for high cholesterol.

The authors found a positive association between total cholesterol (TC) and serum concentrations of PFOS, PFOA, and PFNA. TC is the sum of low-density and very low-density lipoproteins ("bad" cholesterol) and high-density lipoproteins ("good" cholesterol). The findings appeared driven by an increase in the non–high-density lipoprotein fraction of TC, and the association was most pronounced for PFNA. In contrast, PFHxS concentrations were inversely related to TC: samples reflecting the highest PFHxS exposure had the lowest TC levels.

The authors observed little evidence of associations between body size, insulin resistance, and PFC concentrations. They note several limitations in this study, including the fact they could not rule out the possibility of reverse causality—that is, that having higher cholesterol levels could lead to increased PFC concentrations in the blood. Nevertheless, the results support previous epidemiologic research indicating that environmentally relevant exposures to PFCs may affect human cholesterol metabolism or homeostasis.

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